

Reply to Blazer *et al.*: Flawed challenges to “Acetylcholinesterase inhibitors and Gulf War illnesses”

Blazer *et al.* (1) challenge my PNAS article (2) connecting acetylcholinesterase inhibitor (AChEi) exposure and Gulf War veterans' (GWV) illness (GWI).

Excess amyotrophic lateral sclerosis (ALS) in GWV was not represented as central to the inferences drawn (ref. 2, p. 4299); moreover, the ALS excess is shown by not one but three independent studies (3–5) (including two in the supporting information). Although rarity of ALS reduces power for risk factor identification, mounting evidence supports a role for AChEi-relevant exposures (pesticides, paraoxonase genotypes, regulating organophosphate detoxification) in sporadic ALS (6–8). ALS remains rare and not a dominant contributor to neurological deaths, although a significant ALS excess is still important.

Lack of EMG/NCV abnormalities “in numerous large, representative, controlled, investigations” of GWV (for which they cite one study with 49 symptomatic veterans) is incompatible how? No evidence suggests that EMG/NCV abnormalities follow low-level AChEi exposure either.

The assertion that the article did not “pay any attention to recall bias” in epidemiological studies is false: I expressly stated “the results may be influenced by self-report bias” (p. 4295) (subsuming recall bias) and also exposed other study flaws that “limit confidence in causal inferences across AChEi

classes from epidemiological studies viewed in isolation” (p. 4296). Moreover, when airing relative advantages of genetic/enzyme studies, I note that those are (in contrast) “difficult to ascribe to recall or reporting bias” (p. 4296).

I agree that my conclusions differed from prior reports. It is true too that I considered only original evidence and not opinion or authority: the mischaracterizations of the article throughout by Blazer *et al.* (1) ably illustrate why, when primary sources are available, secondary representations of evidence should be eschewed.

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The author declares no conflict of interest.

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